REMARKS/ARGUMENTS

Claims 1-48 are canceled. New claims 49-60 are added. Hence, claims 49-60 are now active in this application.

Applicants wish to thank Examiner Brian Gangle for the recent helpful and courteous discussion conducted with their U.S. representative. In accordance therewith, it was clarified that the claim amendments of July 10, 2007, have been entered. Further, it was clarified that although only the CRF is missing from the official file in the U.S. Patent and Trademark Office that Applicants would also submit a new hard copy of the Sequence Listing, Amendment directing entry thereof into the specification, and sworn statement. It was clarified, however, that all of these materials were previously submitted on July 10, 2007.

Claim 33 stands rejected under 35 U.S.C. 102(e) as being anticipated by Doucette-Stamm et al. at (U.S. 6,699,703). However, this reference fails to either disclose or suggest the claimed invention.

Notably, claim 49 pertains to the peptide fragments of the recombinant protein derived from PBP2x.

The cited reference merely discloses a PBP2x protein.

Thus, the peptide of claim 49 which is a fragment of a truncated PBP2x protein, the truncated PBP2x protein containing 536 amino acids of PBP2x plus 4 to 28 amino acids from the linking peptides, is easily distinguishable from the full-length 750 amino acid protein of the cited reference.

Furthermore, one skilled in the art would be neither motivated nor enabled from the cited reference to prepare the recombinant protein of claim 49 as the artisan would have no guidance from the reference to combine the truncated PBP2x protein fragments as claimed.

Hence, this ground of rejection is unsustainable and should be withdrawn.

Claims 23-26, 28-33 and 48 stand rejected under 35 U.S.C. 112, first paragraph, as the disclosure therefore is said to be non-enabling.

Claims 23-26, 28-33 and 48 also stand rejected under 35 U.S.C. 112, first paragraph, as the disclosure ostensibly fails to comply with the written description requirement.

However, both of these grounds of rejection are deemed moot for the following reasons.

I. Written Description

1. The recombinant protein of the claimed invention (designated "mini-PBP2x") contains concatenated fragments of a PBP2x protein of *Streptococcus pneumoniae*; the four fragments of said PBP2x protein of *S. pneumoniae* being situated at positions corresponding respectively to position 74-90, 186-199, 218-228 and 257-750, and each fragment is preceded by linking peptide of 1 to 7 amino acids.

2. It is clear from the specification that PBP2x is a well-known protein of *S. pneumoniae*. The encoding gene (*pbpX* gene) has been identified (see page 6, lines 10 to 14) and numerous PBP2x protein sequences from different isolates of *S. pneumoniae* are available in the sequence data bases (see the accession numbers indicated in Annex 1). The structure, including the 3D structure, as well as the structure-function relationship of the PBP2x have been determined (see page 3, line 7 to page 4, line 3 of the specification).

3. The sequence of the PBP2x of other isolates may be obtained by conventional molecular biology techniques, according to standard protocols which are well-known in the art. For example, the nucleic acid sequence encoding the PBP2x protein is amplified by PCR, RT-PCR and/or cloned by screening genomic DNA libraries by hybridization with homologous probe, as specified page 11, lines 26 to 29 of the specification. Primers suitable for the PCR or RT-PCR amplification are disclosed page 11, lines 29 to 31 and in the sequence listing. Given the sequence conservationof PBP2x as mentioned below, these primers are suitable for amplifying the PBP2x coding sequence from any strain of *S. pneumoniae*.

4. The present application discloses the amino acid sequence of the four fragments of the PBP2x protein of the strain R6 of *S.pneumoniae* and their position relative to the PBP2x amino acid sequence (figure 1).

5. PBP2x sequence alignments (see the BLAST in Annex 2) clearly indicates that the PBP2x protein is very conserved (86 % identity). Furthermore, no gaps were found between the different PBP2x sequence (see Annex 2).

6. Therefore, the skilled artisan could easily and straightforwardly obtain directly the sequence of the four fragments of the claimed recombinant protein for any PBP2x.

7. In addition, the sequence of the linking peptide is specified in the present application; the linking peptide may consist of homologous sequence (i.e., amino acids flanking the fragments in the PBP2x amino acid sequence (see page 5, lines 26 6o 32) or heterologous sequences (small amino acids : A, S, G or T; see page 6, lines 3 to 6).

8. The recombinant protein of the claimed invention is produced by conventional molecular biology techniques, according to standard protocols which are well-known in the art. For example, the nucleic acid sequence encoding the PBP2x protein is amplified by PCR, RT-PCR and/or cloned by screening genomic DNA libraries by hybridization with homologous probe, as mentioned above in item 3. The recombinant protein is derived from the PBP2x protein by standard mutagenesis techniques. For example, the deletion of the PBP2x sequences and the insertion of the linking peptide may be carried by site-directed mutagenesis on a phagemide, followed by PCR amplification of the mutagenised sequence and cloning in an expression vector, as described for example page 12, lines 1 to 9 and in example 1 of the instant application.

Thus, as specified here above, the claimed recombinant protein contains four completely defined fragments of a protein whose sequence, structure and structure-function relationship are well known, and each fragment is preceded by a linking peptide whose sequence is specified in the instant application.

Therefore, the present application adequately describes the invention; indeed as specified here above. Hence, the present specification reasonably conveys and discloses to a person skilled in the art the subject-matter claimed, particularly in view of the following considerations:

- level of skilled and knowledge in the art
- complete or partial structure
- physical and/or chemical properties
- functional characteristics
- correlation between structure and function
- method of making.

For all of these reasons, the specification clearly provides a written description for the claimed recombinant protein which satisfies 35 U.S.C. 112, first paragraph. In essence, the present specification provides more than adequate written description to "allow persons of ordinary skill in the art to recognize that [the inventors] invented what is claimed. In re Gosteli, 10 U.S.P.Q. 2d 1614 (Fed. Cir. 1989). 35 U.S.C. 112, first paragraph requires no move than this.

II. Enablement

In addition to what is specified here above pertaining to the written description, the recombinant protein of the invention (mini-PBP2x) contains mutations in the non penicillin binding domain (or n-PB: positions 50 to 265); the penicillin-binding domain/transpeptidase domain (positions 266 to 615) which represent the major target for identifying novel antibiotics active on beta-lactam resistant strain of *S. pneumoniae* is intact in the recombinant protein of the invention.

Furthermore, example 2 which disclose a mini-PBP2x derived from the PBP2x of the strain R6 of *S. pneumoniae*, clearly desmonstrates that the enzymatic activity of PBP2x (binding to beta-lactams and transpeptidase activity) is still present in the mini-PBP2x and equivalent to that of previous PBP2x mutant (PBP2x*) having a deletionof the cytoplasmic and transmembrane domains of PBP2x only (deletions of residues 1 to 48).

Since all the PBP2x proteins from different strains of PBP2x are very conserved and share the same structure which correspond to the same function, it is similar results will be obtained with any PBP2x protein.

Therefore, the results obtained with the mini-PBP2x derived from the strain R6 of *S. pneumoniae* are representative of the functionality of all the recombinant proteins as encompassed by the claims.

Thus, the present specification with the general knowledge at the time the claimed invention was made, would have provided the skilled artisan with the information necessary to prepare the claimed recombinant protein.

For these reasons, it is clear that the claimed subject matter is enabled by the present specification.

Additionally, attached hereto is the Rule 132 Declaration of Dr. Thierry Vernet (Annex 3).

Notably, in the Declaration, Dr. Vernet avers that in view of the numerous observations made in the Declaration that the present specification provides both an adequate written description and enablement of the claimed invention.

In particular, Dr. Vernet is of the opinion that the claimed invention has an adequate written description, i.e., is fairly described by the present specification because:

1) The claimed recombinant protein (named "mini-PBP2x") is well-described in the present specification;

2) PBP2x, itself, is a well-known protein, and the encoding gene (*pbpx gene*) has been identified, and numerous PBP2x protein sequences from different isolates of *S. pneumoniae* are available in sequence data bases (see Annex 1);

3) the sequences of PBP2x of other isolates maybe easily obtained by conventional methodologies;

4) the present specification describes the amino acid sequences of the four fragments of the PBP2x protein of the strain R6 of *S. pneumoniae* and their position relative to the PBP2x amino acid sequence (Fig. 1);

5) the present specification specifies the linking peptide sequence;

6) PBP2x protein is very conserved; and

7) the skilled artisan would, thus, be put in possession of the sequences of the four fragments of the claimed recombinant protein for any PBP2x.

Dr. Vernet is also of the opinion that the claimed invention is adequately enabled by the present specification because:

1) Example 2 of the present specification demonstrates that the enzymatic activity of PBP2x (binding to beta-lactams and transpepticdase activity) remains present in the mini-PBP2x and is equivalent to that of previous PBP2x mutant (PBP2x*) having a deletion of the cytoplasnic and transmembrane domains of PBP2x only;

2) all PBP2x proteins from different strains of PBP2x are highly conserved, and share the same structure corresponding to the same function-thus, similar results would be expected with any PBP2x protein;

3) the results obtained with the mini-PBP2x derviced from the strain R6 of *S. pneumoniae* are representative of the functionality of all of the recombinant proteins as encompassed by the claims; and

4) the confirmation of the description in the present specification and the background knowledge and skill of the artisan would have been more than adequate to enable the artisan to practice the claimed invention when the application was filed.

Clearly, both of the above grounds of rejection are moot.

Claims 23-26, 28-33 and 48 stand rejected under 35 U.S.C. 112, first paragraph.

However, it is clear in view of the above remarks and attached Annexes that this grand of rejection is mott.

However, in view of the above claim amendments, this ground of rejection is moot.

Thus, in view of the new claims presented, remarks and Rule 132 Declaration of Dr. Vernet, it is believed that all grounds of rejection under 35 U.S.C. 112, first and second paragraphs, are now moot.

SUPPORT FOR AMENDMENT

All of the new claims are fully supported by the claims and disclosure as originally filed.

SEQUENCE REQUIREMENTS

Please find attached a new sequence listing and CRF version wherein the sequences of more than 4 amino acids which are disclosed in the specification page 6, lines 17 to 24 (sequences M1 to M7 (SEQ ID Nos: 10 to 16)), page 10, line 9 (SEQ ID No: 17) and in figure 1 (top line corresponding to the sequence of PBP2x of *S. pneumoniae* strain R6 : SEQ ID No: 18) have been added.

Note that the sequences of one, two or three amino acids which are presented in page 6, line 24; page 17, lines 17-18; page 18; lines 5, 12, 19 and 26 of the specification are not included in the sequence listing since they are not considered as sequences according to the Standard for the International PCT Applications.

Note also that the bottom line sequence presented in figure 1 corresponds to SEQ ID No.1.

"(SWISSPROT P14677 or GENBANK 18266817)" and "(SWISSPROT P14677)" which are erroneous have been replaced by "(corresponding to the nucleotide sequence GenBank X16367)" in the following passages of the specification : page 5, lines 15-16; page 7, line 3; page 8, line 23; page 16, line 11; page 16, Table I; page 17, lines 11-13; page 19, lines 16-17 and in the abstract. Support for this modification is found on page 17, lines 10 to 13.

A readily apparent error in the sequence SEQ ID No. 1 of the sequence listing has been noted. It clearly emerges from the overall specification and for example from the legend of figure 1 (page 16, lines 8 to 15) and Table I (page 16), that SEQ ID No. 1 corresponds to the mini-PBP2x derived from the PBP2x of the strain R6 which is presented in figure 1. The mini-PBP2x of figure 1 has a methionine (M) in position 186. Therefore, the threonine (T) which is present at that position in SEQ ID No. 1 should be replaced by a methionine (M).

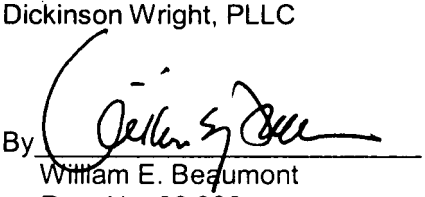
This error has been corrected in the attached substitute sequence listing. Accordingly, it is believed that the present application is now in consideration for allowance. Early notice to this effect is earnestly solicited.

Applicants hereby petition for the Commissioner to charge any additional fees or any underpayment of fees which may be required to maintain the pendency of this case or credit any overpayment to Deposit Account No. 04-1061.

Respectfully submitted,

Dickinson Wright, PLLC

Date: October 2, 2007

By 
William E. Beaumont
Reg. No. 30,996

DICKINSON WRIGHT, PLLC
1901 L Street, N.W.
Suite 800
Washington, DC 20036-3506
Tel. 202/659-6929
Fax: 202/659-1559